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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/203,004	02/28/94	BERD	D TJU1156

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EXAMINER	
UNGAR, S	
ART UNIT	PAPER NUMBER
1806	18

DATE MAILED: 02/04/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on AMENDMENT Filed November 25, 1996.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or ~~thirty days~~, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-7, 10, 22-38 is/are pending in the application.

Of the above, claim(s) 1, 29-33 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 2-7, 10, 22-28, 34-38 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 15

☑ Interview Summary, PTO-413 3 Sheets

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

★ U.S. GPO: 1996-410-238/40050

1. Claims 2-7, 22-28 and 34-38 are pending in this application. Claims 1 and 29-33 have been cancelled and Claims 34-38 have been added. Claims 2-7, 10, 22-28 and 34-38 are currently under prosecution.

2. The Art Unit location and the examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1806.

3. WITHDRAWAL OF FINALITY OF LAST OFFICE ACTION TRANSITIONAL APPLICATION UNDER 37 CFR 1.129(A)

Since this application is eligible for the transitional procedure of 37 CFR 1.129(a) and the fee set forth in 37 CFR 1.17(r) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.129(a). Applicant's first submission after final filed on November 27, 1995 (Paper No. 16) has been entered.

2. Applicant's amendment, filed November 25, 1996 (Paper No. 16) is acknowledged. Claims 8 and 9 were amended on page 2 of Paper No. 16. It is noted that Claims 8 and 9 were cancelled in Paper No. 6 filed January 17, 1995.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

4. The specification is objected to under 35 USC 112, first paragraph, and Claims 22-28, 34-38 , 2-7 and 10 stand rejected under 35 USC 112 first paragraph as failing to provide sufficient guidance to enable one skilled in the art to use a pharmaceutical composition comprising a hapten modified human

tumor cell for treating cancer, where the tumor cells are selected from either autologous or allogenic cells and the tumor is selected from the group consisting of melanoma, breast, lung, colon, kidney and prostate. The specification specifically teaches a melanoma vaccine and describes immune responses to the melanoma vaccine and clinical results (p 19-43). While the specification states that cancers treatable with the present invention include those listed above, the specification does not teach how to select tumor cells which would be effective in treating these other cancers.

The claims stand rejected for the reasons previously set forth in Paper No. 7, page 5, paragraph 3 through page 7, paragraph 2 and in view of the lack of sufficient guidance in the specification which would force one of skill in the art into undue experimentation in order to use the invention as claimed. The rejection is maintained for the reasons previously set forth in Paper No. 10, Page 10, paragraphs 2-3.

6. The specification is objected to under 35 USC 112, first paragraph, and Claims 22-28, 34-38 , 2-7 and 10 are rejected under 35 USC 112 first paragraph as failing to provide sufficient guidance to enable one skilled in the art to use a pharmaceutical composition comprising a hapten modified human tumor cell for treating cancer, where the tumor cells are selected from either autologous or allogenic cells and the tumor is selected from the group consisting of melanoma, breast, lung, colon, kidney and prostate.

The sentence bridging pages 27-28 in the specification states that "All vaccines were DNP-conjugated and mixed with Bacille Calmette-Guerin"

(BCG). Claim 22 was amended in Paper No. 16, on page 2, filed November 29, 1995, to exclude the recitation of an adjuvant. However, it appears that including BCG may be a critical step for the reasons disclosed in Paper No. 7, page 7, paragraph 2 through page 8, paragraph 1. In addition, the specification does not provide guidance for using a pharmaceutical composition in which the melanoma cells are not irradiated. It would be expected that irradiation would be necessary to prevent the cells from growing following injection for the reasons disclosed in Paper No. 7, page 7, paragraph 2. Claim 1, which was amended, on page 2 of Paper No. 8 to read "A method for treating melanoma .....comprising administering.....a composition comprising an irradiated composition ....comprising.a mixture of tumor cells" was cancelled in Paper No. 16. In view of the cancellation of the language "irradiated composition" and the amendment of claim 22 in Paper No. 16, claims 22-28, 34-38 , 2-7 and 10 are rejected for the reasons previously set forth in Paper No. 7, pages 7-8.

7. The specification is objected to under 35 USC 112, first paragraph, and Claims 22-28, 34-38 , 2-7 and 10 are rejected under 35 USC 112 first paragraph as failing to provide sufficient guidance to enable one skilled in the art to use a pharmaceutical composition comprising a hapten modified human tumor cell for treating cancer, where the tumor cells are selected from either autologous or allogenic cells and the tumor is selected from the group consisting of melanoma, breast, lung, colon, kidney and prostate.

The specification discloses that all vaccines were DNP-conjugated. The specification does not provide guidance for using a pharmaceutical composition in which the melanoma cells are not conjugated to the hapten for the reasons disclosed in Paper No. 7, page 8, paragraph 2. This rejection was originally made in paper No. 7, page 8 but was withdrawn in Paper No. 10 when claim 22 was amended in Paper No. 9, page 3 to recite a "composition....comprising.....conjugated to a hapten". In view of the amendment to claim 22 excluding the recitation os "conjugated to a hapten" presented in Paper No 16, the rejection of the claims has been reinstated.

8. The specification is objected to under 35 USC 112, first paragraph, and Claims 22-28, 34-38 , 2-7 and 10 are rejected under 35 USC 112 first paragraph as failing to provide sufficient guidance to enable one skilled in the art to use a pharmaceutical composition comprising a hapten modified human tumor cell for treating cancer, where the tumor cells are selected from either autologous or allogenic cells and the tumor is selected from the group consisting of melanoma, breast, lung, colon, kidney and prostate for treating cancer.

The composition is contemplated as a vaccine against cancer that will stimulate an immune response against cancer (see specification pages 17 and 18). The specification gives guidance on and exemplifies compositions wherein the hapten is DNFB, DNCB and DNP. However, the claims read on any hapten, regardless of size or chemical composition. There is no exemplification of or guidance on how a person skilled in the art would use a hapten selected from all available haptens to induce an appropriate immune response that would

treat cancer. The specification does not address the pharmacokinetic properties of these haptens *in vivo* nor does it provide guidance as pertains to the appropriate doses and conditions necessary to carry out the process leading to an appropriate immune response against cancer. In view of the above and in view of the lack of predictability associated with the appropriate production of an immune response using a hapten in the variety of tumors encompassed within the scope of the claims one of skill in the art would be forced into undue experimentation in order to carry out the claimed invention.

9. Claims 2-7, 10, 22-28 and 34-38 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite because there is no antecedent basis for the phrase "said tumor" in claim 36 from which it depends.

Claim 4 is indefinite because there is no antecedent basis for the phrase ""and extracts" in claim 36 from which it depends.

Claims 22-28 34, 35 and 38 are indefinite because Claim 22 is drawn to a composition, yet the only component recited is the a hapten modified human tumor cell. Minimally, the claim should include an (pharmaceutically) acceptable carrier. The specific function, the (therapeutically) effective amount of the active ingredient and the (pharmaceutically) acceptable carrier can all be included.

Claims 22-28, 34, 35 and 38 are indefinite because Claim 22 recites "a hapten modified human tumor cell" . The claim is confusing because it does not

recite how the cell has been modified. Is the hapten conjugated to the cell? has it been internalized into the cell?

Claim 23 is indefinite because there is no antecedent basis for the phrase "said tumor...extracts" in claim 22 from which it depends.

Claim 24 is indefinite because there is no antecedent basis for the phrase "said tumor" in claim 22 from which it depends.

Claims 25 and 25 are indefinite because there is no antecedent basis for the phrase "said tumor" in claim 22 from which it depends.

Claims 2-7, 10 and 36-37 indefinite because Claim 36 is drawn to a composition, yet the only component recited is the a hapten modified human tumor cell. Minimally, the claim should include an (pharmaceutically) acceptable carrier. The specific function, the (therapeutically) effective amount of the active ingredient and the (pharmaceutically) acceptable carrier can all be included.

Claims 2-7, 10 and 36-37 are indefinite because Claim 36 recites "a hapten modified human tumor cell" . The claim is confusing because it does not recite how the cell has been modified. Is the hapten conjugated to the cell? has it been internalized into the cell?

Claim Rejections - 35 USC § 102

10. Claims 2-7, 22-28, and 34-38 are rejected under 35 U.S.C. § 102(a) as being anticipated Murphy et al for the reasons previously set forth in Paper No. 7, page 10.

It is assumed for examination purposes that a hapten modified human tumor cell is a tumor cell conjugated to a hapten because Berd et al, (IDS Item AA) define a hapten-modified autologous vaccine as human melanoma tumor cells conjugated to the hapten DNP.

This rejection was withdrawn in Paper 10, page 3 in view of the amendment of the claims. However, in view of the amendment of the claim 22 presented in Paper No. 16, the rejection of these claims has been reinstated .

11. Claims 2-7,- 22-28 and 34-38 are rejected under 35 U.S.C. § 102(a) as being anticipated Berd et al for the reasons previously set forth in Paper No. 7, page 11.

This rejection was withdrawn in Paper 10, page 3 in view of the amendment of the claims. However, in view of the amendments of the claims presented in Paper No. 16, the rejection of these claims has been reinstated .

Claim Rejections - 35 USC § 103

12. Claims 2-7, 10, 22-28 and 36-38 are rejected under 35 U.S.C. § 103 as being unpatentable over Berd et al or Murphy et al in view of Geczy et al for the reasons previously set forth in Paper No. 7, pages 12 and 13.

This rejection was withdrawn in Paper 10, page 3 in view of the amendment of the claims. However,in view of the amendments of the claims presented in Paper No. 16, the rejection of these claims has been reinstated .

13.. The Declaration of Dr. David Berd, Paper No. 14, filed November 25, 1996, has been received and entered. Dr. Berd's declaration has been fully considered but does not overcome the rejections of the claims. Dr. Berd

maintains that as a skilled artisan, he would expect DNP to be representative of all haptens in general for use in the present invention. The argument has been noted but not found to be persuasive for the reasons set forth above in paragraph 7.

Response to Applicant's Amendment

2. The following rejections are being withdrawn:

(i) Rejections of claims 1 and 29-33 under 35 USC 112, first paragraph, because the claims have been cancelled.

(2) Rejection of Claims 1-7, 10 and 22-33 under 35 USC 112, second paragraph, because of the amendments of the claims recited in Paper No. 16.

Applicants arguments filed November 25, 1996 (Paper No. 16), in conjunction with the Berd declaration under 35 CRF 1.132, filed November 25, 1996 (Paper No. 14) have been fully considered but are not found convincing.

Claims 1-7, 10 and 22-33 stand rejected under 35 USC 112, first paragraph for the reasons set forth above in paragraph 5.

Applicant argues that "a declaration of a person skilled in art addressing a question of fact should be considered by the Examiner" and that Dr. Berd provides facts in support of melanoma representing other tumors in general and also attests to the recognition that DNP is representative of haptens in general and other haptens are expected to perform equivalently to DNP. The argument has been noted but not found to be persuasive because it is contrary to the teachings of Bystryn as disclosed in Paper No. 7, page 6, paragraph 1 who teaches that for cancer immunotherapy to be effective, the immune responses

induced must be directed to antigens being expressed by the tumor being treated. Bystryn discloses the pattern of tumor antigens expressed by cancers of the same histological type in different individuals vis variable. Bystryn also teaches that there is variation in the pattern of tumor antigens expressed by different tumor cells of the same histological type in the same individual. Furthermore, the profile of tumor antigens expressed by a tumor during its progression may be altered by the immune response of the host as a result of antigenic modulation. Bystryn also discloses that as a consequence of this variability it is unlikely that vaccines prepared from a single tumor antigen will be effective against a broad range of tumors of the same histological type a and for the same reasons autologous vaccines may not be effective against other tumor cells in the same patient. As disclosed on Page 7 of Paper No. 7, Hellstrom et al disclose that allogeneic tumor cells used as immunogens may not induce cytotoxic lymphocyte response because there may be a lack of major histocompatibility complex matching between the immunogen and the patient's lymphocytes. For the reasons discussed above, a vaccine composition for the treatment of one type of cancer cannot be extrapolated to other types of cancer and the effectiveness of either allogenic or autologous tumor antigens in treating cancer is highly unpredictable. Further, the argument in support of DNP as a representative of haptens in general has been noted but found to not be persuasive for the reasons stated in paragraph 8 of this action.

Claims 1-7, 10 and 22-33 stand rejected under 35 USC 112, first paragraph for the reasons set forth above in paragraph 6.

Applicant argues that the present invention is directed to a composition comprising a haptenized tumor cell and method of treating cancer comprising administering the composition and that the selection of melanoma cells and the representation of melanoma as equivalent to other tumor types is set forth in the specification as well as in the Declarations filed. The argument has been considered but not found persuasive for the reasons stated above.

Finally, Dr. Berd discusses the prior art as it pertains to the instant invention. The arguments have been fully considered but are not persuasive because Dr. Berd does not address the teachings of the references of record.

14. No claims allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached at (703) 308-2731. The fax phone number for this Art Unit is (703) 308-4065.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Susan Ungar
January 27, 1997

LILA FEISEE
SUPERVISORY PATENT EXAMINER
GROUP 1800